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DEVICE THROUGH WHICH PARTICLES CAN PASS, FOR SEPARATING SUBSTANCES USING POROUS, FLAT, ADSORPTION MEMBRANES

Description

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The invention concerns a particle passing apparatus for the carrying out of material separation by means of the permeation of liquids through more than one layer of porous, flat adsorption membranes.

By the term, "porous, flat adsorption membranes", (i.e. a membrane adsorber) microporous, flat membranes are to be understood , which possess on their surface functional groups and/or ligands or reactants, which have the capability for exchange action with at least one substance of a liquid phase which is in contact with said membrane (WO-A1-92-00805, Sartorius, AG). The transport of the liquid phase through the adsorption membranes is convective. The designation "adsorption membranes" is a general term for various kinds of adsorption membranes such as ion exchange membranes, ligand membranes, affinity membranes and activated membranes. These so designated membranes themselves are subdivided in accord with their functional groups, ligands and reactants into various adsorption membrane types.

The apparatuses in accord with the invention can be installed for the treatment of particle bearing liquids, as these occur, for example, in biological technology, in chemical and food industries, or in water treatment or in wastewater handling.

In this way, for example, biologically active substances are produced by cell cultures. For the obtaining of the said active substances, the cells must be, as a rule, removed and separated by means of centrifuging and/or filtration, so that, from the remaining liquid, the desired material can be isolated.

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For the avoidance of this additional step in particle separation, K. H. Kroner et al. describes a procedure for crossflow filtration with adsorption-affinity membranes for the primary separation of proteins in an example of the isolation of the enzyme malate dehydrogenase from E-coli and baker's yeast with the aid of a Cibacron blue modified membrane (Bioforum 12, 455-458 (1992)). In the execution of the process, the particle loaded fluid flow was caused to proceed directly to the cell remnant run-off by tangential flow over one membrane layer. The targeted substance found in the filtrate collected in the said membrane. After the removal of the particles by washing the membranes, the targeted substance was recovered by suitable solvents. A disadvantage of this procedure, lies in the non-uniform permeation of the target substance through the one membrane layer. This disadvantage can be overcome by a cross-flow filtration apparatus as shown in Fig. 12 of DE-PS 197 11 083. However, this still possesses a disadvantage, in that it must be driven by a high energy input, so that, first, a higher permeate flow is assured and second, a sufficient overflow velocity for the entrainment of the particles with the fluid flow is achieved. Otherwise, the first membrane would be blocked and the entire permeation process defeated. In comparison, the dead-end filtration units disclosed by DE-PS 197 11 083 and DE-OS 44 32 628, exhibit, because of the use of a plurality of layers of porous, adsorption membranes, a uniform throughput of the targeted substance at a high adsorption capacity. However, in this case, the liquid feed must, in any case, be particle free, in order to prevent a blockage of the filtration units.

Thus, the invention has the purpose, of creating an apparatus for the carrying out of material separation by means of a permeation of particle carrying liquids through porous adsorption membranes, which characterizes itself by a high adsorption capacity, a uniform throughput of the target material and a simple construction.

This purpose is achieved by the object of Claim 1

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Surprisingly, it was discovered, that substance separation by means of adsorption membranes, even with liquids bearing a heavy load of particles, could be realized, if the equipment has more than one layer of porous, flat adsorption membranes. Such membranes are to be distanced, one from the other and possess at least one opening or preferably, a plurality of openings, for the passage of particles. In operation, the first layer of porous membrane, which has at least one opening, is subjected to a flow, under pressure, of a particle laden liquid from which a material therein dissolved is to be separated. A first portion of the liquid permeates particle-free through the pores of the first layer of the membrane, whereby the target material is adsorbed in the interior of the said membrane. The remaining portion of the liquid, together with the particles, flows through the at least one hole of the first layer into that space which is created between the first and the next spatially separated layer, wherein it joins the permeate which simultaneously has penetrated the membrane. The so united portions of the liquid can now flow over the surface of the second layer of the flat, adsorptive membrane, until the portion carrying particles flows through the at least one hole of this second membrane. Again, in the same manner as above, a portion of the liquid permeates particle free through pores of this second membrane. Both portions of the liquid now collect together in the space created by the separation of the second and the next layers. This described process repeats itself so often, until that liquid of the joined liquids of the particulate laden portion and the permeate exit from the final layer of the flat, adsorption membrane through the at least one hole therein. At this point, the liquid exiting from the particle passing device is completely, or nearly, totally freed of the target material.

In the case of a plurality of holes, these are arrayed in a regular or irregular arrangement in the membranes of the equipment. These holes have such an opening size, that passage therethrough by the particles in the liquids is possible. The diameter of the said holes runs as a multiple of the nominal pore diameter of the employed microporous adsorption membranes. The holes should be, however, smaller than 100-times the diameter of the largest particle in the liquids. For an optimal employment of the entire

membrane volume for adsorption, it has shown itself as advantageous if the said holes in neighboring

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layers are offset one from the other. This is true even when the number of the holes in a membrane unit is not large and/or they are of small diameter. The least fraction that a hole can take, relative to the area of a layer of the membrane, would run from 20 % down to 4 %. The holes can be made be optionally in shape, advantageously, they can be in the shape of a slot or a circle with a diameter of 0.01 to 20 mm, preferably, 0.5 to 2 mm. The neighboring layers of the porous flat adsorption membranes, by means of spacer elements, are arranged parallel to one another with a gap between them in a range of 0.1 to 5 mm, preferably between 0.2 to 1 mm. For spacers, consideration can be given to webs, gratings, webbing, knitted material or matting, which characterize themselves by a favorable ability to pass particles.

The flat adsorption membranes should have a pore diameter in a range between 0.1 to 10 μm, with preference given to 3 to 5 μm. Adsorption membranes with smaller pore diameters exhibit too restricted a permeability for practical usage, whereas in the case of adsorption membranes with large pores, the danger of blockages by the impingement of smaller particles exists. Flat membranes are employed as adsorption membranes, which carry functional groups and/or ligands or reactants, which have the capability for an exchange activity which removes from the liquid at least one material, preferably the targeted material.

The apparatus can be constructed as a flat module or, in an advantageous embodiment of the invention, also as a wound module. Particularly advantageous is a modular cylindrical embodiment, as this is described in DE-PS 197-11-083.

The invention shall now be more closely examined and described with the aid of the drawings 1 to 4. There is shown in:

Fig. 1 schematically, a section through one embodiment of the invented device,

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Fig. 2 one version of an arrangement of holes in a layer of a flat adsorption membrane,

Fig. 3 a curve of a typical material separation and

Fig. 4 an exploded presentation of another embodiment of the arrangement of the holes in adjacent layers of the flat adsorption membrane.

In accord with Fig. 1, the particle passing device 1 comprises a housing 2 with a liquid inlet 3 and a liquid outlet 4. In the housing 2 are to be found more than one layer of porous adsorption membranes 5, arranged in such a manner, that during operation of the device, 1, the liquids from the inlet 3 to the liquid outlet 4 must sequentially pass the said layers. The layers of the adsorption membrane 5 are provided with holes 6 for the passage of the particles 8 borne in the feed liquid 7. For the sake of clarity, only few holes 6 are shown. The layers of the adsorption membranes 5 are sealingly covered in their peripheral rim areas next to the housing 2 by means of a sealant 9. The layers of the adsorption membrane 5 are distanced, one from the other, for the creation of a space 10 for the collection of a first portion 11 of the liquid 7 which has permeated through the adsorption membrane, and also so distanced for the remaining second portion of the particle laden liquid which has passed through the holes 6 of the layers 5. The offset distance of the layers of the adsorption membrane 5 is stabilized by means of spacers 13, which may be in the form of particle passing gratings, mesh, knitted material or matting placed between the layers 5. For better flowing conditions, the first layer 5 and for a better collection of the fluid 7 after the last layer of the adsorption membrane 5, appropriate flow guidance apparatuses, namely in the form of the said spacers 13 are furnished.

The explosion type presentation of Fig. 4 shows an additional embodiment of the arrangement of the holes 6 in the sequentially spaced layers of the flat adsorption membranes 5 as well as the thereto attendant spacers 13. These elements are, for instance, installed in a (not shown) housing with liquid inlet/outlet fittings and again sealed at the edges.

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Example 1

Two meters of a 6 cm wide, strongly basic adsorption membrane of the type SARTOBIND® Q (Sartorius, AG) were provided with holes in an arrangement such as presented in Fig. 2. The holes were spaced from each other at a distance of 1.8 cm and were of diameter 3.5 mm. The holes took up an area of 1.8 % of the area of the frontal membrane surface. This membrane strip was worked up together with a 6 cm wide mesh band of propylene to make a cylinder module in accord with DE-PS 197 11 083.

The cylinder module received, by means of a tube-pump, one liter, at a pH value of 8.3, of a particle laden liquid (the feed solution) of a commercially available bovine serum albumin (BSA) – of the firm of Kräber, Hamburg – and air dried bakers yeast in a buffer of the composition of 0.01 M tris (hydroyl-methyl) amino methane (TRIS), along with concentrated hydrochloric acid. The feed rate was 0.6 l/min. The liquid leaving the cylinder module was conducted through a flow photometer of the firm of Wedgewood, San Carlos, USA. The absorption of the solution was determined to be 280 nm and was continually recorded. After the passage of the liter of liquid, the device was washed with the buffer until the absorption of 280 nm was reduced to read 0 nm. Subsequently, first the BSA was eluted from the cylinder module with a solution of 0.25 M sodium chloride in the buffer and finally the bound yeast removed by 1M sodium chloride in the buffer. During the entire procedure, no significant increase of the pressure occurred. Thereafter, the cylinder module stood available for an addition cycle. The example was repeated.

Fig. 3 shows the typical curve of such an experiment. An immediate break through of the yeast particles occurred through the cylinder module, as is represented by the steep climb at the start of the curve.

After the washing out of all UV-absorbing particles, the BSA was eluted with 0.25 M NaCl in the buffer (first large peak in the curve), and then the yeast, still retained in the cylinder module was desorbed by with 1 M NaCl in the buffer to give the second peaking. The dynamic binding capacity (reaching of 10 % of the concentration of the

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added BSA solution in the run-off) proved to be 0.38 mg/cm^2 membrane surface. The static binding capacity was 0.5 mg/cm^2 membrane surface. The following results were achieved:

First Run:

Fraction	Volume [l]	Absorption [E 280 nm]	Turbidity	BSA [g]	Recovery of BSA [%]
Feed sol.	1	0.6	+	1	—
0.25 M NaCl	0.58	0.8	-	0.8	80
1 M NaCl	0.5	not meas	+	not meas	—

Second Run

Fraction	Volume [l]	Absorption [E 280 nm]	Turbidity	BSA [g]	Recovery of BSA [%]
Feed sol.	1	0.6	+	1	—
0.25 M NaCl	0.58	0.66	-	0	6
1 M NaCl	0.5	not meas	+	not meas	—

Example 2

In an additional example 10 g air dried commercially obtainable baker's yeast was suspended in one liter of the buffer described in Example 1 and this suspension was conducted in a circulation in the cylinder module as indicated in Example 1. The average entry pressure was 0.1 bar and did not change itself significantly during the 30 minute time to run the example. Thereafter to the suspension, 1 g BSA was added and this mixture run through the cylinder module.

After freely washing, as described above in the Example 1, the BSA was eluted with 0.25 M NaCl in the buffer.

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At this point, 0.41 g BSA were recovered. Therewith, the dynamic binding capacity was reduced by 48 %.

The cylinder module was then washed with 1 M NaCl in the buffer, and then treated with 1 M NaOH and allowed to stand for 10 minutes. Subsequently a wash was carried out with 1 M NaOH and thereafter again with 1 M NaCl and finally washed with only the buffer.

The cylinder module was again charged with BSA. The following results were achieved:

Third run

Fraction	Volume [l]	Absorption [E 280 nm]	Turbidity	BSA [g]	Recovery of BSA [%]
Feed sol.	1	0.6	+	1	—
0.25 M NaCl	0.5	1.06	-	0.86	86
1 M NaCl	0.5	not meas	+	not meas	—

The static binding capacity ran still 90 % of the value of that of the first run of Example 1.